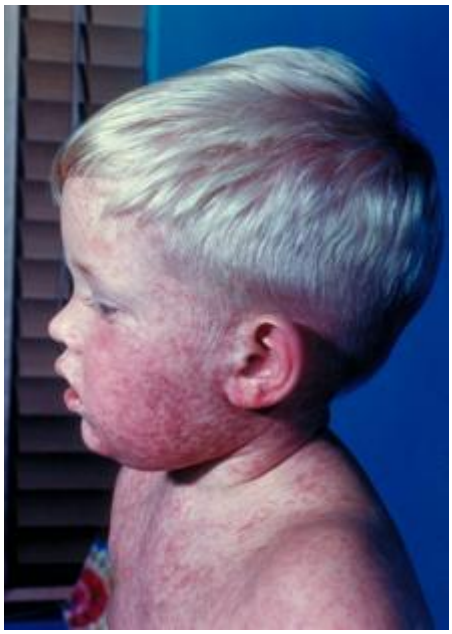
MEASLES (RUBEOLA)
Report Immediately

✓DISEASE AND EPIDEMIOLOGY

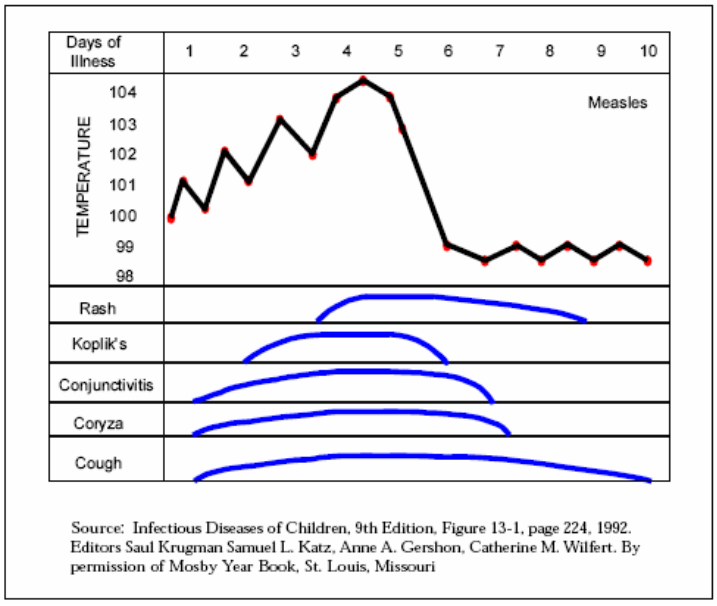
Clinical description:

Measles is an acute viral illness characterized by a prodrome followed by a maculopapular rash.



- The *prodrome* lasts 2-4 days (range 1-7 days). It is characterized by fever, often peaking as high as 103°–105°F, with malaise (tiredness), cough, coryza (runny nose), or conjunctivitis.
- The *rash* is maculopapular and usually lasts 5–6 days. It begins on the face, and over the next few days extends to the body and extremities. The lesions increase in size and may coalesce (come together). Initially, lesions blanch (lose color) with fingertip pressure. By day 3-4 of the rash, however, most do not blanch with pressure. The skin over the more severely affected areas may slough off. The rash fades first on the face and head, and then disappearing from the body and extremities.
- *Koplik spots*, blue-white spots that generally develop on the mucosa of the mouth, are a characteristic sign of measles disease. Koplik spots appear 1–2 days before the rash to 1–2 days after the rash.
- Other symptoms associated with measles include anorexia (loss of appetite), diarrhea (especially in infants), and generalized lymphadenopathy (disease of the lymph nodes).

The time course of clinical events in measles infection.



Source: Infectious Diseases of Children, 9th Edition, Figure 13-1, page 224, 1992. Editors Saul Krugman Samuel L. Katz, Anne A. Gershon, Catherine M. Wilfert. By permission of Mosby Year Book, St. Louis, Missouri

Persons with measles usually present with characteristic disease. However, two forms of measles infections that have abnormal presentations have been described. *Atypical measles* occurs only in persons who were vaccinated with inactivated measles vaccine and are subsequently exposed to wild-type measles virus. An estimated 600,000 to 900,000 persons received the inactivated measles vaccine in the United States from 1963 to 1967. The inactivated measles vaccine sensitizes recipients to measles virus antigens without providing protection. Atypical measles is characterized by fever, pneumonia, pleural effusions, and edema. The rash appears first on the wrists or ankles and is usually maculopapular or petechial, but may have urticarial, purpuric, or vesicular components. Atypical measles may be prevented by revaccinating with live measles vaccine. Moderate to severe local reactions with or without fever may follow vaccination; these reactions are less severe than with infection with wild measles virus. *Modified measles* occurs primarily in persons who received immune globulin (IG) as post-exposure prophylaxis and in young infants who have some residual maternal antibody. It is characterized by a prolonged incubation period, mild prodrome, and sparse, discrete rash of short duration. Similar mild illness has been reported among previously vaccinated persons.

Diarrhea, otitis media (ear infection), and pneumonia (viral or bacterial) are the most common complications. Subacute sclerosing panencephalitis (SSPE) is a very rare degenerative central nervous system disease believed to be due to persistent measles virus infection of the brain. Generally, SSPE appears 7 years after measles infection. Symptoms include progressive deterioration of behavior and intellect, followed by ataxia (awkwardness), seizures, and eventually death. Hemorrhagic measles, which rarely occurs in the US, is characterized by high fever (105°–106°F), seizures, delirium, respiratory distress, and hemorrhage (bleeding) into the skin and mucous membranes. Encephalitis, seizures, and death can also occur, although rarely. Pneumonia is the most common cause of death in measles cases. Complications are seen in roughly 30% of all measles cases, and generally occur more frequently in children under 5 years of age and adults over 20 years of age. Measles illness during pregnancy results in a higher risk of premature labor, spontaneous abortion (particularly in the first trimester), and low-birthweight infants.

Causative agent:

Measles is caused by a single-stranded RNA paramyxovirus. Two envelope proteins, F (fusion) and H (hemagglutinin), play an important role in pathogenesis. The F protein is responsible for fusion of the virus to the host membrane, viral penetration, and hemolysis. The H protein is responsible for adsorption of the virus into the host cell. There is only one antigenic type of measles virus.

Differential diagnosis:

The differential diagnosis includes, but is not limited to, rubella, fifth disease, enterovirus or adenovirus infection, mononucleosis, scarlet fever, roseola, Kawasaki's disease, Rocky Mountain spotted fever, and drug reaction.

See **Clinician's Guide to Measles Diagnosis**, for guidance on diagnosing measles.

Laboratory identification:

Because of the rarity of measles in the US and the fact that most clinicians have never seen a case, laboratory diagnosis is essential. IgM and IgG serology, viral culture, and RT-PCR should *all* be performed for highly suspect cases.

Serology:

All serum samples should be tested for both IgM and IgG to assist in identifying false positive IgM tests. There are two methods for serological testing: direct capture and indirect capture. All but one commercially available tests are indirect capture tests. Indirect capture requires that serum samples be processed prior to testing to remove IgG and rheumatoid factor. Incomplete removal or problems with processing the sample can lead to false positive results. The direct capture method, which is used by CDC, measures IgM directly from the serum sample, without any sample processing needed. Direct capture tests are considered confirmatory. In all measles serology tests, indirect and direct, rheumatoid factor and parvovirus, rubella, or roseola infections can cause false positive measles IgM because of cross-reactivity. Serum samples should be collected *at least* 3 days (72 hours) after rash onset for IgM titers to reach the threshold level. IgM titers are detectable for at least 28 days after rash onset. A high positive IgG in conjunction with a low positive IgM is most likely a false positive result, indicating that IgG was not fully removed prior to testing with the indirect capture method. If a negative IgM test is received on a case where the sample was collected in the first 3 days (72 hours) after rash onset, another sample should be collected and tested. Test interpretation should be supplemented by a good description of the clinical course of illness in the suspected case.

Viral Culture:

Virus isolation and genetic characterization can take several weeks to complete, and therefore should not be used as a routine method to diagnose measles. However, virus isolation is important in determining the geographic origin of the virus, and collecting clinical specimens for viral isolation should be done at the same time as samples taken for serologic testing. Specimens for viral culture should only be tested once serological results come back positive for measles. Urine and throat or nasopharyngeal swabs are appropriate specimens for viral culture. Virus is present in throat, NP, and oropharyngeal specimens within the first 3 days of rash onset. Virus is present in urine a few days before and a few days after the rash appears. Specimens for viral culture should be collected for every highly suspect case, but should only be tested once serology results are positive. Samples should be forwarded to the Utah Public Health Laboratory (UPHL), where they will be kept until preliminary serological results are available. Submission to CDC should be coordinated through UDOH epidemiologist.

RT-PCR:

Along with viral culture, RT-PCR can determine the geographic origin of the virus. However, RT-PCR can take several weeks to perform and should not be used for initial diagnosis. Urine and throat or nasopharyngeal swabs are appropriate specimens for viral culture. Virus is present in throat, NP, and oropharyngeal specimens within the first 3 days of rash onset. Virus is present in urine a few days before and a few days after the rash appears. However, a negative culture or RT-PCR does not rule out measles because the tests are not very sensitive and are much affected by the timing of specimen collection and the quality and handling of the clinical specimens. Specimens for viral culture should be collected for every highly suspect case, but should only be tested once serology results are positive. Samples should be forwarded to the Utah Public Health Laboratory (UPHL), where they will be kept until preliminary serological results are available. Submission to CDC should be coordinated through UDOH epidemiologist.

See **Guide to Laboratory Testing and Interpretation** for guidance on interpreting serology results. See **CDC Protocol for Measles Virus Isolation** for instructions on properly obtaining clinical specimens for virus isolation.

Treatment:

There is no specific treatment for measles. In children that are immunocompromised or severely ill, the measles virus has demonstrated susceptibility to ribavirin. In communities with a known vitamin A deficiency, a child diagnosed with measles should be administered vitamin A.

Case fatality:

Measles is the leading vaccine-preventable killer of children worldwide. In developing countries, case-fatality rates average 3–5%, but can range as high as 10–30% in some localities.

Reservoir:

Humans are the only known hosts of measles virus.

Transmission:

Measles is primarily spread through respiratory droplets generated by coughing and sneezing and by direct contact with nasal or throat secretions of infected persons. However, airborne transmission of much smaller particles has been documented in closed areas for up to 2 hours *after* the infected person has left. Measles is considered one of the most contagious diseases in the world.

Susceptibility:

Anyone can get measles, however it is typically regarded as a childhood disease. Vaccination efforts have eradicated the virus in the United States. All cases in the United States are either imported from an area where the measles virus is still circulating, usually Europe or Asia, or are linked to a case with imported measles virus. Measles cases can occur throughout the year, but tend to peak in late winter and spring.

Incubation period:

The incubation period from exposure to prodrome averages 10-12 days. From exposure to rash onset averages 14 days (range 7-18 days).

Period of communicability:

Measles is contagious four days before rash onset to four days after rash onset. More than 90% of susceptible contacts will develop disease.

Epidemiology:

Since 1997, the incidence of measles in the U.S. has been very low, with fewer than 200 cases reported each year. A record low annual total of 44 cases were reported in 2002. The last case of measles in Utah occurred in 2002.

All individuals may be at risk for measles, but those most at risk are generally limited to five groups:

1. Children <12 months of age (those who are too young to be immunized);
2. Unimmunized individuals;
3. Adults who may have received an earlier ineffective measles vaccine prior to 1968 or who are unimmunized because they graduated from school prior to mandatory measles vaccination;
4. Children and adults with only one dose of measles-containing vaccine; and
5. Those who are foreign born and have never been vaccinated or did not have measles as a child in their country of origin.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Promote vaccination to prevent disease.
- Identify all cases and susceptible exposed people rapidly.
- Identify the source of infection through genotyping of viral isolates
- Assist in the international effort to eradicate measles.

Prevention:

Vaccination is the primary method of prevention.

Chemoprophylaxis:

Vaccination within 72 hours of exposure in unimmunized persons can provide protection against measles in some cases. For persons whom vaccination is contraindicated (immunocompromised, pregnant women, and infants less than one year of age) IG can provide some protection – either by preventing or reducing the severity of disease. IG should be administered within 6 days of exposure, preferably within 72 hours. If immunization status is unknown, vaccination in an already immune person is not harmful.

Vaccination:

Two doses of measles-containing vaccine (MMR) separated by at least 28 days, are routinely recommended for all children. The first dose is given at 12-15 months of age; the second is given at 4-6 years of age. The immunity level among recipients of 2 doses of vaccine is 99%.

MMR is a live, attenuated vaccine, and therefore pregnant women and persons with an impaired immune system should not receive the vaccine. Nonpregnant women should avoid becoming pregnant within 28 days after the last dose of vaccination. Breastfeeding is not a contraindication for MMR vaccination.

Some persons mistakenly believe that the MMR vaccine causes autism. The first recognizable signs of autism generally appear around one-year of age, which coincidentally is the same time children receive the first dose of MMR vaccine. Carefully performed scientific studies have found only a temporal (time) association between these two events, and no causal relationship between MMR vaccine and autism.

Isolation and quarantine requirements:

Isolation: Persons diagnosed with measles should voluntarily isolate themselves at home until 7 days after rash onset.
Hospital: Any resident diagnosed with measles should be put into airborne isolation for the duration of the illness. Transportation of the patient should be limited.
Quarantine: Close contacts should have their immunization records audited for appropriate immunity. A person is considered susceptible unless they have documentation of 2 doses of measles vaccine administered at least 1 month apart or they were born prior to 1957. A verbal report of immunization is not considered adequate documentation. If adequate documentation cannot be provided, the person should be considered susceptible. Susceptible persons should be vaccinated immediately, preferably within 72 hours after exposure. Once vaccinated, a person may come out of quarantine immediately. Susceptible persons, if not immunized within 72 hours after exposure, should be quarantined in their home until 21 days after the onset of rash in the last measles case. If immunization status is unknown, vaccination in an already immune person is not harmful.

R396-100-8. Exclusions of Students Who Are Under Exemption and Conditionally Enrolled Status.
(1) A local or state health department representative may exclude a student who has claimed an exemption or who is conditionally enrolled from school attendance if there is good cause to believe that the student has a vaccine preventable disease and:
(a) has been exposed to a vaccine-preventable disease; or
(b) will be exposed to a vaccine-preventable disease as a result of school attendance.
(2) An excluded student may not attend school until the local health officer is satisfied that a student is no longer at risk of contracting or transmitting a vaccine-preventable disease.

✓CASE INVESTIGATION

Reporting:

If measles is at all suspected, it should be reported immediately to the local health department or the Utah Department of Health.

Case definition:

Measles (2007):

Clinical Case Definition

An illness characterized by all the following:
- A generalized rash lasting greater than or equal to 3 days,
- A temperature greater than or equal to 101.0°F (greater than or equal to 38.3°C), and
- Cough, coryza, or conjunctivitis.

Laboratory Criteria

- Positive serologic test for measles immunoglobulin M antibody, or
- Significant rise in measles antibody level by any standard serologic assay, or
- Isolation of measles virus from a clinical specimen.

Case Classification

Suspect: Any febrile illness accompanied by rash.
Probable: A case that meets the clinical case definition, has noncontributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed case.
Confirmed: A case that is laboratory confirmed (does not need to meet the clinical case definition) or meets the clinical case definition and is epidemiologically linked to a confirmed case.

Epidemiologic classification:

Internationally imported case:

A case in which measles results from exposure to measles virus outside the United States as evidenced by:

- At least some of the exposure period (7–21 days before rash onset) occurring outside the United States,
- Rash onset occurring within 21 days of entering the United States, and
- No known exposure to measles in the U.S. during that time.

U.S.-acquired case:

A case in which the patient:

- Had not been outside the United States during the 21 days before rash onset or
- Was known to have been exposed to measles within the United States.

U.S.-acquired cases are further classified into four mutually exclusive groups:

Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.
Imported-virus case: A case for which an epidemiologic link to an internationally imported case was not identified, but for which viral genetic evidence indicates an imported measles genotype, i.e., a genotype that is not occurring within the United States in a pattern indicative of endemic transmission. An endemic genotype is the genotype of any measles virus that occurs in an endemic chain of transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.
Endemic case: A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥12 months within the United States.
Unknown source case: A case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S.

Case investigation process:

All highly suspect cases of measles warrant immediate action. Cases of measles should be managed as follows:

- Local and state health departments should be immediately notified.
- Appropriate laboratory samples and preliminary clinical and epidemiologic information (including vaccine history and travel history) should be obtained.
- Strict isolation should be imposed until 7 days after rash onset.
- All case contacts should be identified and appropriately managed (explained in detail below).
- The source of the exposure should be identified.

See **Measles Protocol - Case Management**, for guidance on assessing the likelihood of a measles diagnosis.

Outbreaks:

A single case of measles is considered an outbreak. Identify all close contacts and define population groups at specific risk and immunize. An epidemiologically linked case is one in which the patient has had contact with one or more persons who have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

Identify case contacts:

Close contacts are people who have either been exposed to the case or exposed to the case's respiratory secretions during the case's infectious period (4 days before rash onset to 4 days after rash onset). Consider members of the following groups:

- Household and family members;
- Those who have direct contact with respiratory secretions;
- Healthcare workers with face-to-face contact with a patient;
- Core groups of close friends, social contacts, boyfriends, girlfriends;
- School/daycare contacts;
- Contacts at church activities and employment;
- Participants in extracurricular activities (such as fieldtrips); and
- Persons exposed at social events.

Case contact management:

Because of the contagiousness of the disease, active identification of all contacts of a measles case is warranted. When cases are identified, it is public health's responsibility to:

- Assess contacts' immunity by auditing immunization records. Contacts must be able to produce documentation of vaccination – a verbal history of vaccination is not sufficient.
- Vaccinate susceptible contacts. Susceptible contacts not immunized within 72 hours after exposure should be quarantined in their home until 21 days after the onset of rash in the last measles case.
- Work with susceptible contacts' physicians to determine if administration of IG is necessary.
- Provide educational materials informing of exposure and recommending vaccination.

See **Measles Protocol - Contact Management**, for detailed guidance on managing contacts.

✓REFERENCES

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